

Remarks

Claims 1-3, and 7-46 are pending. Claims 19-33 and 35-46 were previously withdrawn. Claim 6 is canceled by this communication. Claims 1-3, 7-18 and 34 are rejected.

Information Disclosure Statement

Entries A59 and 60 in the returned Information Disclosure Statement (IDS) filed on September 22, 2005 were marked by the Examiner without the Examiner's initials or signature. Applicants respectfully request the Examiner to initial or otherwise sign off these two entries.

Note, the same request was presented in the response to final office action mailed on July 17, 2007. Since the Examiner takes no action on the request, Applicants assume the above two entries were considered by the Examiner.

Rejections under 35 U.S.C. 112

Claims 1-3, 7-18 and 34 are rejected as being indefinite under 35 U.S.C. §112, 2nd paragraph. Applicants believe the amendments to the claims cure these deficiencies.

Rejections under 35 U.S.C. 103

Claims 1-3, 7-18 and 34 are rejected under 35 U.S.C. 103(a) as being obvious over Wang in view of U.S. Patent No. 5,620,738 to Fan et al. ("Fan").

Claimed Invention

Claims 1, 15 and 34 are independent claims.

Claim 1 defines a method for immobilizing an anti-thrombogenic material into a coating comprising a base coat layer posited on a surface of an implantable medical device within the mammalian body. The method requires (a) preparing a base coat

mixture comprising a binding material, a grafting material, a photoinitiator, and a solvent; (b) applying the base coat mixture directly to the implantable medical device; (c) polymerizing the base coat mixture to form the base coat layer on the medical device by photopolymerization; (d) applying a formulation comprising the anti-thrombogenic material to the surface of the base coat layer; and (e) immobilizing the anti-thrombogenic material directly to chemically functional groups in the binding material within the base coat layer on the surface of the medical device. The binding material of the base coat layer is selected from oxirane compounds, and acetoacetoxy compounds. The anti-thrombogenic material is selected from glycosaminoglycans, superoxide dismutase mimetic (SODm), or combinations thereof.

Claim 15 defines a method for end-immobilizing an anti-thrombogenic material into a coating comprising a base coat layer posited on a surface of an implantable medical device for use within a mammalian body. The method comprises (a) preparing a base coat mixture comprising a binding material, a grafting material, a photoinitiator, and a solvent; (b) applying the base coat mixture directly to the implantable medical device; (c) polymerizing the base coat mixture to form the base coat layer on the medical device by photopolymerization; (d) applying a formulation comprising the anti-thrombogenic material to the surface of the base coat layer; and (e) end-immobilizing the anti-thrombogenic material, through a group that terminates the anti-thrombogenic material, directly to chemically functional groups in the binding material within the base coat layer on the surface of the medical device. The binding material of the base coat layer is selected from oxirane compounds, and acetoacetoxy compounds. The anti-thrombogenic

material is selected from glycosaminoglycans, superoxide dismutase mimetic (SODm), and combinations thereof.

Claim 34 defines a method for immobilizing an anti-thrombogenic material into a coating comprising a base coat layer posited on a surface of an implantable medical device for use within a mammalian body. The method comprises (a) preparing a base coat mixture comprising a binding material, a grafting material, a photoinitiator, and a solvent; (b) applying the base coat mixture directly to the implantable medical device; (c) polymerizing the base coat mixture to form the base coat layer on the medical device by photopolymerization; (d) applying a formulation comprising the anti-thrombogenic material to the surface of the base coat layer; and (e) immobilizing the anti-thrombogenic material directly to chemically functional groups in the binding material within the base coat layer on the medical device. The binding material of the base coat layer is selected from oxirane compounds, and acetoacetoxy compounds. The wherein the anti-thrombogenic material is selected from glycosaminoglycans, superoxide dismutase mimetic (SODm), and combinations thereof.

Wang

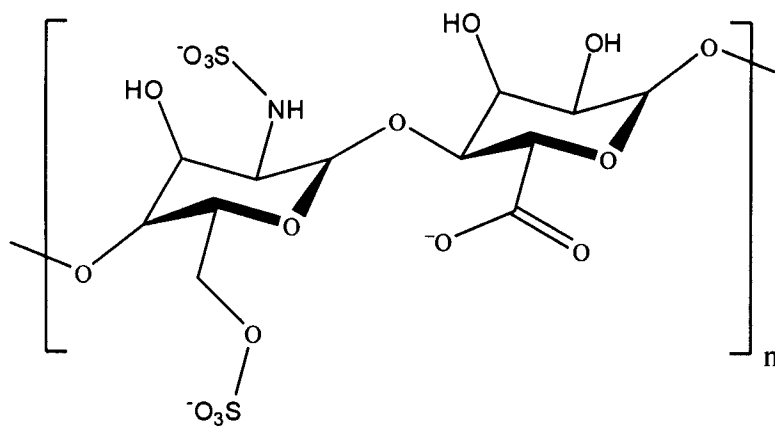
Wang describes a method of coating a polymeric substrate by exposing the substrate with a photo initiator, generating reactive radical sites on the surface of the substrate, contacting the substrate with a composition comprising a monomer, and grafting the monomers onto the substrate by forming covalent bonding at reactive radical sites on the substrate surface (col. 3, lines 52-64; col. 4, line 57 through col. 6, line 47).

Wang does not describe or teach a binding material in addition to grafting monomer materials.

The Examiner alleges that Wang teaches a crosslinker in the coating composition that would act as the binding material as defined in claim 1 (Office Action, page 4, middle). Applicants respectfully submit that the Examiner misreads Wang. At col. 8, lines 30-40, **Wang indicates that the crosslinker is a diacrylate crosslinker. As a person of ordinary skill in the art would recognize, in the grafting procedure provided by Wang, this diacrylate will be activated by the UV to crosslink with a remaining vinyl group(s) in the coating.** Upon completion of grafting, this diacrylate will **no longer exist in its molecular form and no longer active.** Therefore, contrary to the Examiner's assertion, the crosslinker cannot not act as the binding material as defined by claim 1. Indeed, at col. 11, lines 18-27, Wang indicated that agents can be **ENTRAPPED** within the graft layer. This is consistent with the two examples of the antithrombogenic compounds, benzalkoniumheparinate and trididecylmethylammonium heparinate in that these two heparinates are chemically inert with respect to forming covalent bonds since the heparinate moiety in these compounds are ionic moieties. While Wang at col. 11, lines 29-33 goes on to state that the entrapment can be with or without covalent interactions between the agents and the functional groups that may or may not exist on the graft layer, Wang certainly fails to provide chemical means to cause this covalent interaction between the agent and the graft layer to occur. As a person of ordinary skill in the art would recognize, to covalently attach an agent to a coating, both the coating and the agent have to include chemically active groups such that under a set of right conditions, the chemically active groups in the agent and the coating would undergo a chemical reaction to form a covalent bond between them. As the above discussion shows, the crosslinker in the coating composition in Wang, upon UV initiated graft

polymerization, would become chemically inert, for the UV initiated polymerization would cause the crosslinker to lose its vinyl functionality in polymerization. The exemplary antithrombogenic agents disclosed in Wang are also chemically inert with respect to forming covalent bonds. As such, the entrapment of the antithrombogenic agent in the graft layer in the coating disclosed by Wang is one without covalent bonding.

In the Office Action, page 4, last line, the Examiner states that end-immobilization with the heparin compound, benzalkoniumheparinate and trididecylmethylammonium heparinate, can occur via the pendant amine group in the compounds. Applicants respectfully submit this statement is unfounded. Heparin has a structure of



and thus, contrary to

the Examiner's assertion, there is no pendant amine groups in a heparin compound. The sulfamide groups in benzalkoniumheparinate and trididecylmethylammonium heparinate are ionic groups and will not form covalent bonding with the graft layer in Wang. Amine groups can be attached to heparin, but this will happen only if one takes action to achieve so.

In sum, Wang does not describe or teach immobilizing an antithrombogenic material to a base coat via a binding material.

Fan

Fan describes a process to provide a lubricious coating on a device by applying a hydrophilic polymer to a binder polymer (col. 1, lines 40-51). **The binder polymer are polymers or copolymers from a monomer comprising a vinyl moiety and a carboxylic acid moiety** (col. 1, lines 48-51). The hydrophilic polymer and the binder polymer, via the carboxylic acid moiety, are bonded together by hydrogen or ionic bonds (col. 4, line 40-45). Note, Fan indicates that the bonding between the hydrophilic polymer and the binder polymer is substantially free from covalent bonding (col. 4, lines 54). In addition, Fan specifically indicates that the binding polymer is substantially free, e.g., less than 1% of highly reactive functional moieties such as isocyanate, aldehyde and epoxy moieties (col. 4, lines 50-54). At col. 1, lines 56-58, Fan states that the coating disclosed therein is made lubricious “without the need ... to covalently bond the hydrophilic polymer to the surface of the substrate.” Therefore, **Fan not only fails to provide a binding material that provides for immobilization of an antithrombogenic material, but also clearly teaches away from such a binding material.**

Accordingly, claims 1, 15 and 34 are non-obvious and patentably allowable over Wang in view of Fan under 35 U.S.C. 103(a). Claims 2, 3 and 7-14, which depend from claim 1, and claims 16-18, which depend from claim 15, are also patentably allowable over Wang in view of Fan under 35 U.S.C. 103(a) for at least the same reason.

Claims 1-3, 7-18 and 34 are rejected under 35 U.S.C. 103(a) as being obvious over WO 38546.

WO 38546 describes immobilizing a general therapeutic, diagnostic or hydrophilic agent onto a coating using a binding material. The binding material does not

include any of oxirane compounds and acetoacetoxy compounds. As a person of ordinary skill in the art would recognize, different binding materials would have different chemical activities and thus would require the antithrombogenic material to have different functional groups so as to attach or immobilize the antithrombogenic material to a coating through the binding material. For example, a binding material with an amino group, which is a base, and one with a carboxylic acid group, which is an acid, would require totally opposite chemically functional groups on the antithrombogenic material. Therefore, claims 1, 15 and 34 are patentably allowable over WO 38546 under 35 U.S.C. §103(a). Claims 2, 3 and 7-14, which depend from claim 1, and claims 16-18, which depend from claim 15, are also patentably allowable over WO 38546 in view of Fan under 35 U.S.C. 103(a) for at least the same reason.

The undersigned authorizes the examiner to charge any fees that may be required or credit of any overpayment to be made to Deposit Account No. **07-1850**.

CONCLUSION

Withdrawal of the rejection and allowance of the claims are respectfully requested.

If the Examiner has any suggestions or amendments to the claims to place the claims in condition for allowance, applicant would prefer a telephone call to the

undersigned attorney for approval of an Examiner's amendment. If the Examiner has any questions or concerns, the Examiner is invited to telephone the undersigned attorney at (415) 393-9885.

Date: January 24, 2008
Squire, Sanders & Dempsey L.L.P.
One Maritime Plaza, Suite 300
San Francisco, CA 94111
Telephone (415) 393-9885
Facsimile (415) 393-9887

Respectfully submitted,

/ZLI/
Zhaoyang Li, Ph.D., Esq.
Reg. No. 46,872